REMARKS

Claims 1-72 are pending in this application and subject to a restriction requirement.

Restriction is Improper

Claims 1-72 have been subject to restriction by the examiner.

The claims and subject matter associated with each group as alleged by the examiner are as follows (emphasis in original, as provided by the examiner on pages 2-3 of the Office Action dated Apr. 17, 2009):

Group I (Claims 1-19, 41-52):

> A β sheet multimeric cytokine whose sequence has been altered by mutating a residue in a monomer component of the multimeric cytokine protein so as to improve the free energy of the monomer or of the multimeric complex relative to the wild-type unmutated monomer component **so as to be more stable than the wild-type**, unaltered cytokine protein and a method of making said cytokine.

Group II (Claims 20, 21, 23-34, 53-61, 63-69, 71, 72):

> A β sheet multimeric cytokine with selectivity for a target receptor, in which one or more amino acids in the cytokine that are located in the receptor-binding interface are substituted for replacement residues that include amino acid side-chain conformations that are predicted to fit into the binding interface with the target receptor so as to provide an **increase in binding affinity and selectivity/specificity** of the cytokine protein for that target receptor, a method of making said cytokine, [and] methods of using said cytokine to treat cancer.

Group III (Claim 22):

> A β sheet multimeric cytokine with selectivity for one or more target receptors wherein selectivity for a first target receptor is achieved by substituting one or more amino acids in the cytokine for replacement residues so as to **decrease affinity for one or more different target receptors**.

Group IV (Claims 35, 37-40, 62):

> A β sheet multimeric cytokine with selectivity for a target receptor whose sequence has been altered so as to be **more stable than the wild-type**, unaltered cytokine protein and whose sequence has been altered so as to provide and **increase in binding affinity and selectivity/specificity** of the cytokine protein for that target receptor, and a method of making said cytokine.

Group V (Claims 36, 70):

> A β sheet multimeric cytokine with selectivity for two or more target receptors whose sequence has been altered so as to be **more stable than the wild-type**, unaltered cytokine protein and wherein selectivity for a first target receptor is achieved by substituting one or more amino acids in the cytokine for replacement residues so as to **decrease affinity for one or more different target receptors**.

However, the examiner has noted that unity exists between Groups I and IV or Groups II and IV. The examiner has also noted that unity exists between Groups I and V or between Groups III and V.

The claims have been restricted to one or more of the above five groups because the subject matter of the claims allegedly does not relate to a single general inventive concept under PCT Rule 13.1 and because the subject matter of the claims allegedly lacks the same or corresponding special technical features under PCT Rule 13.2. Applicants respectfully disagree and traverse.

Without acquiescing to the restriction requirement, Applicants elect Groups II and IV in order to fully respond to the action.

Applicants assert that restriction is not required in this case. The determination of whether there is a single general inventive concept "shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim." PCT RULE 13.3. Here, applicants have, as they are free to do, presented alternate language in multiple claims to define their claimed subject matter. Applicants respectfully assert that the examiner has not afforded applicants a "broad, practical consideration of the degree of interdependence of the alternatives presented" as required. See MPEP § 1850. Applicants note that lack of unity of invention should not be raised nor maintained on the "basis of a narrow, literal or academic approach." Id. Applicants further note that "the benefit of any doubt being given to the applicant" where the unity of invention is not perfectly clear. Id.

Furthermore, Applicants respectfully disagree with the assertion by the examiner that the alleged special technical features of, for instance, Groups II, III, and IV are proper. For example, the special technical feature of Group III is alleged to be, in essence: "substituting . . . amino acids in the cytokine. . . so as to decrease affinity for . . . target receptors." The

special technical feature of Group II, on the other hand, is alleged to be: "amino acids . . . substituted . . . so as to provide an increase in binding affinity and selectivity/specificity of the cytokine . . . for . . . [a] target receptor." Applicants disagree.

The claims of at least these groups are unified by the recitation of "selectivity." Indeed, increased or enhanced selectivity of a β sheet multimeric cytokine for one or more receptors can be achieved by either a decrease *or* an increase in affinity of the cytokine for its receptor[s]. This is supported in the application as filed. Support for an increase in affinity resulting in increased selectivity is found at least in the claims as originally filed and amended, as the examiner has so noted in the groupings described above. Support for a decrease in affinity in the claims as originally filed and as amended, and in the specification on at least page 20, line 15: "Accordingly, affinity for a receptor may be slightly compromised for improvements in selectivity/specificity."

Applicants further note that claim 35, alleged by the examiner to be properly restricted to Group IV, and claim 36, alleged by the examiner to be properly restricted to Group V, both recite "substituting one or more amino acids in the cytokine . . . so as to provide variants with enhanced . . . selectivity/specificity for the target." Thus, enhanced selectivity is achieved even though the amino acid alterations result in decreased affinity for a receptor; claim 35 (allegedly in Group IV) also recites "so as to decrease affinity for . . . target receptors." Meanwhile, enhanced selectivity is also achieved through amino acid alterations that result in increased affinity for a receptor; claim 36 (alleged Group V) recites "so as to provide an increase in binding affinity . . . for the target receptor."

CONCLUSION

For all of the reasons above, applicants respectfully traverse the restrictions and request withdrawal of the same. If restriction is maintained at all, applicants respectfully traverse and request that Groups II, III, IV, and V be joined as one group as the recitation of achieving "selectivity" in the claims is a unifying special technical feature of the claimed subject matter. If the examiner disagrees, Applicants respectfully traverse restriction of claims into Groups II, III, and IV and request that these groups be joined and examined on the merits. Finally, if the examiner maintains the restriction as presented in the Office Action, Applicants elect Groups II and IV, as noted previously, with traverse.

Date: June 17, 2009

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